

2. (Amended) A ligand profile which is characteristic for a given cell, the ligand profile comprising a representation of at least ten different polypeptide ligands produced in the cell, wherein all of the at least ten different polypeptide ligands bind to a single type of multi-ligand binding receptor present in the cell, wherein the representation characterizes each individual ligand based upon at least two physical or chemical attributes, one of said attributes being mass or mass-to-charge ratio; provided that, if the multi-ligand binding receptor is an MHC class I or class II receptor, at least 500 polypeptide ligands are represented in the ligand profile; and further provided that the ligand profile is a reproducible characteristic of the cell.

3. (Amended) A ligand profile which is characteristic for a given cell, the ligand profile comprising a representation of at least ten different polypeptide ligands produced in the cell, wherein all of the at least ten different polypeptide ligands bind to a single type of multi-ligand binding receptor present in the cell, wherein the representation characterizes each individual ligand based upon at least one physical or chemical attribute, the at least one physical or chemical attribute comprising amino acid sequence; provided that, if the multi-ligand binding receptor is an MHC class I or class II receptor, at least 50 polypeptide ligands are represented in the ligand profile; and further provided that the ligand profile is a reproducible characteristic of the cell.

4. (Amended) A ligand profile which is characteristic for a given cell, the ligand profile comprising ion fragmentation patterns for at least ten different polypeptide ligands produced in the cell, wherein all of the at least ten different polypeptide ligands bind to a single type of multi-ligand binding receptor present in the cell; provided that, if the multi-ligand binding receptor is an MHC class I or class II receptor, at least 100 polypeptide ligands are represented in the ligand profile; and further provided that the ligand profile is a reproducible characteristic of the cell.

5. (Amended) A ligand profile which is characteristic for a given cell, the ligand profile comprising amino acid sequences of at least ten different polypeptide ligands produced in the cell and having distinct core peptides, wherein all of the at least ten different polypeptide ligands

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C1 bind to a single type of multi-ligand binding receptor present in the cell; provided that, if the multi-ligand binding receptor is an MHC class I or class II receptor, at least 100 polypeptide ligands are represented in the ligand profile; and further provided that the ligand profile is a reproducible characteristic of the cell.

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C2 10. (Amended) A method of generating a reproducible ligand profile for a given cell type, which cell type comprises a selected type of multi-ligand binding receptor, the method comprising:

- (a) providing a first sample of the given cell type, wherein the first sample comprises a first plurality of at least ten different native polypeptide ligands bound to the selected type of multi-ligand binding receptor;
  - (b) isolating the selected type of multi-ligand binding receptor from the first sample;
  - (c) separating the first plurality of ligands from the selected type of multi-ligand binding receptor;
  - (d) fractionating the first plurality of ligands;
  - (e) generating a first profile distinguishing among the first plurality of ligands on the basis of at least one chemical or physical attribute;
  - (f) providing a second sample of the given cell type, the second sample being essentially identical to the first sample, wherein the second sample comprises a second plurality of at least ten different native polypeptide ligands bound to the selected type of multi-ligand binding receptor;
  - (g) isolating the selected type of multi-ligand binding receptor from the second sample;
  - (h) separating the second plurality of ligands from the selected type of multi-ligand binding receptor;
  - (i) fractionating the second plurality of ligands;
  - (j) generating a second profile distinguishing among the second plurality of ligands on the basis of the at least one chemical or physical attribute; and
  - (k) confirming that the first profile and the second profile are essentially identical, and together represent a reproducible ligand profile for the given cell type.
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14. (Amended) A method of generating a ligand profile for a given type of cell, comprising:

C3 (a) providing a sample of lysate of the given type of cell, wherein the sample comprises a first plurality of at least ten different native polypeptide ligands bound to a first type of multi-ligand binding receptor and a second plurality of at least ten different native polypeptide ligands bound to a second type of multi-ligand binding receptor;

(b) isolating the first and second types of multi-ligand binding receptors from the sample;

(c) separating the first plurality of ligands from the first type of multi-ligand binding receptor and the second plurality of ligands from the second type of multi-ligand binding receptor;

(d) fractionating the first plurality of ligands and the second plurality of ligands; and

(e) generating a first profile distinguishing among the first plurality of ligands on the basis of at least one chemical or physical attribute and a second profile distinguishing among the second plurality of ligands on the basis of the same at least one chemical or physical attribute.

C4 17. (Amended) A method of comparing a first cell sample to a reference cell sample, comprising:

(a) producing a first ligand profile by a method comprising:

(i) providing a first cell sample comprising a given type of multi-ligand binding receptor bound to a first set of at least ten different native polypeptide ligands;

(ii) isolating the given type of multi-ligand binding receptor and the first set of ligands from the first cell sample;

(iii) separating the first set of ligands from the given type of multi-ligand binding receptor;

(iv) generating a first ligand profile distinguishing among the first set of ligands on the basis of at least one chemical or physical attribute;

(b) providing a reference ligand profile representing a second set of at least ten different native polypeptide ligands extracted from the given type of multi-ligand binding receptor of a

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reference cell sample, wherein the reference ligand profile distinguishes among the second set of polypeptide ligands on the basis of the at least one chemical or physical attribute; and

(c) comparing the first ligand profile to the reference ligand profile, in order to identify differences or similarities between the first cell sample and the reference cell sample.

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21. (Amended) A set of ligand profiles, comprising

(a) a first ligand profile comprising a first representation of a first plurality of at least ten different native polypeptide ligands, all of which bind to at least one multi-ligand binding receptor of a first cell, wherein the first representation distinguishes among the members of the first plurality of ligands based upon at least one physical or chemical attribute; and

(b) a second ligand profile comprising a second representation of a second plurality of at least ten different native polypeptide ligands, all of which bind to the at least one type of multi-ligand binding receptor of a second cell, wherein the second representation distinguishes among the second plurality of ligands based upon the at least one physical or chemical attribute;

provided that (i) the first cell differs from the second cell in a parameter selected from the group consisting of genetic background, culture conditions, genetic background plus culture conditions, *in vivo* exposure to a test compound, and genetic background plus *in vivo* exposure to a test compound; and (ii) any significant difference between the first and the second ligand profiles is attributable to that parameter.

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